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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,892	11/06/2000	Robert H. Austin	4555-107 US	9832

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EXAMINER
BROWN, JENNINE M

ART UNIT	PAPER NUMBER
1755	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/707,892	AUSTIN ET AL.	
	Examiner	Art Unit	
	Jennine M. Brown	1755	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,33 and 35* is/are rejected.

7)☒ Claim(s) *34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Examiner has entered Applicants amendment, which obviates Examiners rejections to claims 5-7, therefore these rejections have been withdrawn.

Newly added claims 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The justification of no new matter as pointed out by Applicants is confusing because materials listed are considered both inert and dielectric materials in the specification. For example, in the specification on p. 8, lines 4-6, "The substrate chip is typically quartz or silicon dioxide ... but other materials and composites now known or later discovered could be used, for example, glass, silicon nitride or polymers. The constrictions may be silicon dioxide, polyimide, PMMA or other suitable *inert* materials...". Later in the specification, Applicants state on page 11, lines 9-13, that "a plurality of dielectric constrictions ... can be formed of *dielectric* material such as quartz or silicone". Examiner is confused as to whether the materials claimed are to be inert, dielectric, neither or both depending on whether or not an electrical field is applied. The specification is unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 10, 13, 15-18, 21, 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063).

Regnier, et al. teach a microfluidic device with a plurality of constrictions (14) separated from one another by a gap (12, 104) and a means for passing polarizable particles in the vicinity of the constrictions by applying a dielectrophoretic field (Figure 4A) to trap particles in the gap (Figures 1A-8; col. 2, l. 1-62; col. 4, l. 61 – col. 5, l. 7; col. 5, l. 37-55; col. 12, l. 53 – col. 16, l. 65). Regnier, et al. teach a fluid input means for inputting fluid (col. 2, l. 29-35). Regnier, et al. teach an electrical signal applied to a pair of electrodes on opposite edges of substrate (col. 9, l. 61-67). Regnier, et al. teach that the constrictions are formed on a substrate using a photolithographic etch (abstract; col. 4, l. 26 – col. 5, l. 36). Regnier, et al. teach that the distance between constrictions is not to exceed 10 to 100 micrometers (col. 4, l. 5-10; col. 7, l. 21-23). Regnier et al. teach a distance between rows of constrictions having varied geometric shapes and those rows can be equally spaced or differently spaced as shown in Figures 1A-6. Regnier, et al teach that the substrate can be quartz and silicon (col. 4, l. 49-51). Regnier, et al. teach that there is a cover plate (13) used which is sealed to the substrate (col. 5, l. 8-23). Regnier, et al. teach through Figure 1A an area of tightly placed constrictions

(top of drawing) next to fewer more widely spaced constrictions (branches towards middle of drawing) to even further spaced apart constrictions (branches towards bottom left hand side of drawing). Regnier, et al. do not teach a dielectric force. Becker, et al. provides evidence that both electrophoretic and dielectrophoretic forces can be obtained by using the same type of apparatus (col. 5, l. 31-33). Becker, et al. teach an electrophoretic apparatus made of glass, silicon dioxide, polymer, ceramic or any suitable electrically insulating material (col. 12, l. 33-41) having inlets and outlets where syringe needle, micropipette, tube or any other suitable device are used to introduce polarizable particles (col. 12, l. 47-49; col. 12, l. 66 – col. 12, l. 1) where the apparatus has electrode arrays controlled by a computer where electrodes can be in two dimensional groupings of columns and rows such that the surface gives an interaction site for the polarizable particles to interact (col. 3, l. 56-67) using electrodes in the array that are individually programmable and addressable by a controller (col. 4, l. 39-46) where the spacing of the electrodes is between 1 micron and 200 microns (col. 5, l. 1-3) and the force used is an inhomogeneous electrical field which is either AC or DC (col. 8, l. 31-47; col. 13, l. 37-49) and can be switched by the controller (col. 13, l. 62 – col. 14, l. 5) whereby the frequency can be generated up to GHz and more particularly between 1 kHz and 10 MHz (col. 17, l. 9-14). Becker, et al. also teach that hydrophobic coatings can be used on the reaction surface (col. 4, l. 16-18) and that the polarizable particles can be moved, fused, merged, mixed, reacted, metered, divided, split, sensed, collected or any combination thereof. The sensing equipment used is either electrical or CCD camera (23; col. 8, l. 14-16).

It would have been obvious to one of ordinary skill in the art to modify the apparatus of Regnier, et al. to use the programmable electrode array of Becker, et al. and the sensing methods of Becker, et al. to trap polarizable particles at the constrictions because one can

programmably manipulate the polarizable particles for different biochemical protocols such as metering, mixing, transporting, division, or other manipulation of fluids so that reagents, intermediates and or final reaction products can be monitored, measured or sensed in parallel or serially in an analytical apparatus to quantitate results, saving time and money.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Kopf-Sill, et al. (US 6358387).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above but do not specifically teach the heating means adjacent said constrictions. Kopf-Sill, et al. teach the use of heating means adjacent to the channels in a microfluidic chip which uses electrofocusing of analytes (col. 9, l. 36 – col. 10, l. 20).

It would have been obvious to one of ordinary skill in the art to add the heating block layer element of Kopf-Sill, et al. to the apparatus of Regnier, et al. in view of Becker, et al. because it would aid in heating or cooling of separated materials for further denaturing, chelating or other reactions where heating or cooling is required so that labeling agents or taggants can be added to a biochemical analyte in order to detect fluorescence in the material.

Claims 5-7, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Walters, et al. (US 6117660).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claims 5-7, Regnier, et al. in view of Becker, et al. specifically teach AC voltages at a predetermined frequency or DC voltage as described previously. Walters, et al. also teach AC or DC voltages at a predetermined frequency for dielectrophoresis (col. 1, l. 49-52) specifically the range of 1Hz (col. 2, l. 39-48; col. 3, l. 23-24; col. 4, l. 7-10, 44-48; col. 5, l. 64-65; col. 6, l. 15-16, 26-28, 34-35; col. 7, l. 13-16, 19-21; col. 10, l. 27-37).

It would have been obvious to one of ordinary skill in the art to use the predetermined AC voltage frequency of Walters, et al. in the apparatus of Regnier, et al. in view of Becker, et al. because it will provide for dielectric pumping of analyte in an electrophoretic apparatus where low temperatures are required and where the coating on the monolithic structures acts similarly to a treated membrane which is used in the electroportation and electrofusion art.

Regarding claim 9, Regnier, et al. in view of Becker, et al. teach using coating moieties of anionic groups, cationic groups, antibodies, antigens and chelation groups which are used to bind things like ssDNA, dsDNA, RNA, cells and polymer particles but do not specifically address biological polymers as the particles being separated. Walters, et al. teach that apparatus for electromanipulation (i.e. electrophoresis) is used on DNA material (col. 2, l. 67), cell membranes (col. 2, l. 6-7) and other materials as discussed in the background of the art (col. 1, l. 13 - col. 10, l. 37). It would have been obvious to one having ordinary skill in the art to specifically separate biological polymers with the device of Regnier, et al. in view of Becker, et al. because biological polymers are specifically responsive to electrophoresis and dielectrophoresis.

Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Austin, et al. (US 5427663).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claim 11, Regnier, et al. in view of Becker, et al. do not specifically teach the height between 0.5 to 5 micrometers. Austin, et al. teach a microfluidic device with the same types of constrictions used by Regnier, et al. in view of Becker, et al. where the height range is between 0.01 and 20.0 micrometers.

It would have been obvious to one of ordinary skill in the art to modify the apparatus of Regnier, et al. in view of Becker, et al. to decrease the height of the apparatus as is stated by Austin, et al. so that the obstacles had a height between 0.01 and 20.0 micrometers because this would constrict the separating mixture to one layer of cells, particles or other analyte to be separated.

Regarding claim 12, Regnier, et al. in view of Becker, et al. state that the preferred distance between the constrictions is 1 micrometer and it would have been obvious to one of ordinary skill in the art to using the reasoning stated regarding claim 11 that the height would need to be large enough to reduce the amount of Joule heating while being small enough to allow only particles of analytes like RNA and DNA to be separated out.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Austin, et al. (US 5427663) or Christel, et al. (US 6368871).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regnier, et al. in view of Becker, et al. do not specifically teach a trapezoidal shape for the constrictions, but it would have been obvious for one of ordinary skill in the art to change the shape of the constriction. Austin, et al. also teach different shapes for constrictions (col. 20, l. 41-44) although trapezoidal shaped is not specifically shown, the arrow shaped constrictions shown in Figure 7 resemble a trapezoidal shape enough that it would have been obvious to one of ordinary skill in the art to substitute a shape change for the constriction because it can easily be changed during the lithography of the substrate. Figures 1b, 1c, 1d and 1f of Christel, et al. show different shapes including trapezoidal (1F). Also the Applicants disclosure does not state any specific advantage that the trapezoidal shape gives over all shapes shown for the configurations and it appears taht the invention would perform equally well using the constriction shapes taught by Regnier, et al., Austin, et al. or Christel, et al. and would have been obvious to one of ordinary skill in the art to use different shaped constrictions, because it would merely be a matter of design choice.

Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regnier, et al. (US 6156273) in view of Becker, et al. (US 6294063) and further in view of Quake, et al. (US 6344325).

Regnier, et al. in view of Becker, et al. teach a microfluidic device as described above.

Regarding claim 19, Regnier, et al. in view of Becker, et al. do not specifically teach one or more channels coupled to the end of the regions for extracting polarizable particles. Quake, et al. teach a microfluidic device having one or more channels coupled to the end of regions for extracting polarizable particles (Figures 1-7; col. 2, l. 39 -56).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. in view of Becker, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions.

Regarding claim 20, Regnier, et al. in view of Becker, et al. do not specifically teach a matrix in a channel downstream from the constrictions capable of fractioning and/or analyzing the particles. Quake, et al. teach fractioning and analyzing the particles separated (col. 2, l. 57 – col. 5, l. 46).

It would have been obvious to one of ordinary skill in the art to combine the channels of Quake, et al. with the constriction based microfluidic apparatus of Regnier, et al. in view of Becker, et al. because the channels will give the user the ability to provide further analysis on the fractionated species from the constrictions because each constriction would be identified by another means such as fluorescent imaging.

Regarding claim 22, Regnier, et al. in view of Becker, et al. teach siloxane substrates as explained previously but do not specifically teach substrate material of polyimide, PDMS or PMMA. Quake, et al. teach PMMA as a substrate resist material deposited on the surface of the substrate.

It would have been obvious to one of ordinary skill in the art to use PMMA photoresist as the etchant material for the substrate because it would have the hydrophobicity required for certain types of wall materials created for the channels of the substrate and is easier to control and cheaper to use than traditional wet etching methods.

Response to Arguments

Applicant's arguments with respect to claims 1-23 and 33-35 have been considered but are moot in view of the new grounds of rejection.

Becker, et al. (US 6294063) was used by Examiner in evidence that both electrophoretic and dielectrophoretic forces can be used to move materials using the same apparatus and it can be used for trapping polarizable particles in the vicinity of the substrate as evidenced in the specification of Becker, et al. supra. Whether the constrictions are viewed as "obstacles" as in the Austin, et al. reference, Examiner points out that a constriction could also be considered an obstacle since it has a length and width which defines a channel space. Examiner also points out that something hooked to the wall of the obstacle is technically trapped by that obstacle, therefore they have the same function. In regard to the Quake, et al. reference, Examiner reminds Applicants that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Applicants admit that the apparatus of Quake, et al. is similar to that of Regnier, et al. because they both teach microchannel arrangement whereby the constrictions taught by Regnier, et al. can be added into a modified microchannel arrangement of Quake, et al. to suggest Applicants apparatus.

Allowable Subject Matter

Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the

base claim and any intervening claims. Prior art of record does not fairly teach or suggest constrictions formed of a material having a dielectric constant substantially less than a buffer in which the particles to be trapped are suspended.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennine M. Brown whose telephone number is (703) 305-0435. The examiner can normally be reached on M-F 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 879-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

jmb
January 24, 2003

Jill Warden
Supervisory Patent Examiner
Technology Center 1700